### Remarks

# I. Status of the Application and Claims

A originally filed, the present application had 11 claims. These were cancelled in a Preliminary Amendment and new claims 12-31 were added. In response to a restriction requirement, claims 22-31 were cancelled and new claims 32-41 were added. In a Response to an Office Action filed by Applicants on August 8, 2008, claims 12-21 and 32-41 were cancelled and new claims 42-62 were added. No claims have been added or cancelled herein.

### II. The Amendments

Claims 43 and 50 were amended to require that reactions have an overall yield of at least 80%. Support for this amendment may be found on page 14 of the application, lines 25-27. No other amendments have been made herein.

## The Rejections

On pages 3-5 of the Office Action, all pending claims are rejected under 35 USC §103 based upon Griengl, et al. (Trends Biotech. 18:252-256 (2000)) in view of the combined teachings of Nagasawa, et al., (Eur. J. Biochem. 267:138-144 (2000)) and Osprian, et al. (J. Mol. Catal. B Enz. 24-25:89-98 (2003)). The Examiner alleges that Griengl teaches the production of enzymatically enriched cyanohydrins by reacting aldehydes or ketones with cyanide in the presence of oxynitrilases. Nagasawa is cited as teaching that nitrilases can be used to convert nitriles to carboxylic acids and Osprian as suggesting the nitrile hydratase/amidase reaction combination. The Examiner alleges that one of skill in the art would have been motivated to combine these references in order to arrive at an efficient catalytic process and that all of the other elements of Applicants' claims would be apparent.

In response to Applicants' previous arguments concerning this rejection, the Examiner states that one cannot show nonobviousness by attacking references individually when they are used in combination. The Examiner acknowledges that two references previously cited by Applicants (US 5,866,379 and US 6,043,061) show that nitrilase by itself may be at least partially inhibited by cyanide-containing compounds but there is no evidence that the reaction resulting from the combined teachings of Griengl, *et al.*, Nagasawa, *et al.* and Osprian, *et al.* would be inoperable.

Applicants respectfully traverse this rejection.

Applicants submit that the Office Action fails to provide a reasonable explanation as to why one of skill in the art would be motivated to combine the various references cited. The Examiner suggests that one of skill in the art would combine the teachings of Griengl, Nagasawa and Osprian to arrive at an efficient process for making enantiomerically enriched α-hydroxycarboxylic acids but, at the same time, seems to acknowledge that the art suggests that that cyanide containing compounds interfere with enzymes involved in carrying out the process. Applicants believe that this is inconsistent and that references teaching that cyanide inhibits enzymes actually suggest that the combination used to reject claims would *reduce* efficiency not increase it. In light of this and the absence of any suggestion in the references themselves, Applicants submit that a motivation to combine has not been established.

A separate consideration is whether, assuming arguendo that the references are combined, those of skill in the art would have a reasonable expectation that the resulting method would be successful. Given the teachings of the inhibitory effect of cyanide compounds, one of skill in the art would, in Applicants' opinion, expect that the combined reactions would result in a decrease in overall yield and efficiency, *i.e.*, that the combination would be *unsuccessful*.

For reasons that are not entirely clear, it appears that the Examiner equates an expectation of operability with an expectation of success. However, Applicants believe that these are not the same and submit that adding a compound to a reaction that reduces yield would not be considered a successful result even if some product is still made. Moreover, Applicants have now added a requirement to claims 43-48 and 50-62 that overall reactions have a yield of greater than 80%. This is clearly something that goes beyond mere operability and which could not be predicted from the references cited.

#### Conclusion

In light of the considerations above, Applicants believe that the Examiner's rejection of claims under 35 USC § 103 has been overcome. It is therefore respectfully requested that

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this rejection be withdrawn and that the claims now pending be allowed. Early notice to this effect is earnestly solicited.

If, in the opinion of the Examiner, a phone call would help to expedite the prosecution of this application, the Examiner is invited to call Applicants' undersigned attorney at (240) 683-6165.

Respectfully submitted, LAW OFFICE OF MICHAEL A. SANZO, LLC

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